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August 25, 1999

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Reference: Docket No. 99D-0529

To Whom It May Concern:

In keeping with the provisions of the Notice published in the Federal Register on June 28, 1999, Alcon Laboratories, Inc. is taking this opportunity to submit official comments regarding the draft guidance for industry entitled "Changes to an Approved New Drug (NDA) or Abbreviated New Drug (ANDA) Application". An original and duplicate of the comments are enclosed.

General Comment: The guidance document does not provide much relief in the submission burden of Industry. The Agency should evaluate supplements received in the past and lessen the burden for those types of supplements that have, historically, always been approved. Supplements that are always approved would appear to be of a nature where risk is sufficiently low and/or are of a type having adequate existing guidance documents, such that a reduced reporting burden would be appropriate.

Specific Comments:

Lines 213-215: Regarding the statement "...had been discontinued and is now being restarted...", the agency should provide clarification as to what constitutes "discontinued". How does the agency propose to establish that a certain type of operation has been discontinued? Does this mean that the capability has been removed from the facility (e.g., manufacturing line dismantled; equipment removed) or that the type of operation has not been actively utilized for some period of time (If so, how long?)? If the site was previously approved for a given type of operation, it seems reasonable to be able to restart that type of operation with revalidation of the site/operations rather than with a Prior Approval (PA) supplement.

Line 374: Deletion of an aseptic processing step should not automatically require a PA supplement, as this change would probably result in less aseptic manipulation and therefore be less invasive to the manufacturing process. There should be an opportunity to handle such a change as a Changes Being Effected (CBE) supplement.

Line 382: Deletion of a piece of equipment from an aseptic processing line should not automatically require a PA supplement as this change could result in less manipulation during the manufacturing process. There should be an opportunity to handle such a change as a CBE supplement.

Lines 389-390: A change from a bioburden based terminal sterilization process to the use of an overkill process would be a change to a less risky process; therefore, the need to submit a PA supplement would be unnecessarily burdensome. A Changes Being Effected in 30 Days (CBE-30) supplement would be sufficient since the agency would have time to review the validation data prior to distribution of product.

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Lines 400-401: As long as there was no impact on acceptance criteria, a change in a filter size would be more appropriately handled as a CBE or CBE-30 supplement than as a PA supplement.

Lines 418-420: Further clarification is requested concerning Prior Approval changes for a drug substance. The use of the term "may" in the guidance statement "may affect impurity profile and/or the physical, chemical, or biological properties" is too broad to provide meaningful guidance.

Lines 442-443: If validation studies demonstrate that there are no product binding problems, then changing from a single sterilizing filter to dual product sterilizing filters should be submitted as a CBE rather than as a CBE-30, due to the fact that such a change represents an increase in sterility assurance.

Lines 638-639: As long as the container/closure seal interface has not been altered, the shape of a container for a sterile drug substance or a sterile drug product should be allowed via submission of a CBE-30 supplement rather than a PA supplement.

The agency's consideration of the foregoing comments will be greatly appreciated.

Respectfully submitted,

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Cc: Sarah Cantrell

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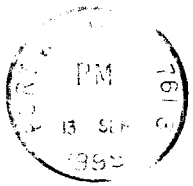

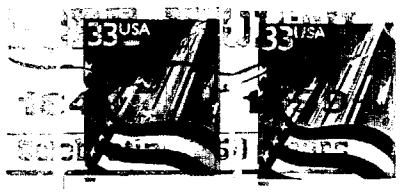

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